UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/041,775	01/10/2002	Eric Brown	P07023US01/BAS	3155

881 7590 04/18/2005

STITES & HARBISON PLLC
1199 NORTH FAIRFAX STREET
SUITE 900
ALEXANDRIA, VA 22314

EXAMINER	
DEVI, SARVAMANGALA J N	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 04/18/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/041,775	BROWN ET AL.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 December 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RESPONSE TO APPLICANTS' AMENDMENT

Applicants' Amendment

1) Acknowledgment is made of Applicants' amendment filed 12/29/04 in response to the non-final Office Action mailed 06/29/04.

Status of Claims

2) Claims 1-16 have been canceled via the amendment filed 12/29/04.

New claims 17-21 have been added via the amendment filed 12/29/04.

Claims 17-21 are pending and are under examination.

Prior Citation of Title 35 Sections

3) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

4) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Objection(s) Maintained

5) The objection to the specification made in paragraph 7 of the Office Action mailed 06/29/04 is maintained for reasons set forth therein and herebelow. Although Applicants amended the specification to correct some trademark recitation(s), others still remain. For example, see line 26 on page 10; and lines 8 and 28 of page 16of the specification.

Objection(s) Moot

6) The objection to claims 9, 11 and 12 made in paragraph 14 of the Office Action mailed 06/29/04 is moot in light of Applicants' cancellation of the claims.

Rejection(s) Moot

7) The provisional rejection of claims 1-4 made in paragraph 8 of the Office Action mailed 06/29/04 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 20 of the co-pending application, SN 09/982,992, is moot in light of

Applicants' cancellation of the claims.

8) The rejection of claims 1-4, 9, 11, 12 and 16 made in paragraph 10 of the Office Action mailed 06/29/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is moot in light of Applicants' cancellation of the claims.

9) The rejection of claims 1-4, 9, 11, 12 and 16 made in paragraph 12 of the Office Action mailed 06/29/04 under 35 U.S.C. § 102(b) as being anticipated by Hook *et al.* (US 5,648,240 - Applicants' IDS) as evidenced by Kaempfer *et al.* (US 2002/0028211A1), is moot in light of Applicants' cancellation of the claims.

New Rejection(s) Based on Applicants' Amendment

Applicants are asked to note the following new rejection(s) made in this Office Action. The new rejections are necessitated by Applicants' submission of new claims.

Rejection(s) under 35 U.S.C. § 112, First Paragraph (New Matter)

10) Claim 19 and the claim(s) dependent therefrom are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

New claim 19 includes the new limitation: 'a condition associated with overstimulation of T cells'. While lines 1-3 of page 8 are supportive of a method of treating or preventing 'pathological' conditions associated with overstimulation of T cells such as toxic shock syndrome, there appears to be no descriptive support for the broad limitation 'a condition associated with overstimulation of T cells', as recited currently. Therefore, the above-identified new limitations in the claims are considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P 608.04 to 608.04(c).

Applicants are respectfully requested to point to the descriptive support in the specification as filed, for the newly added limitations, or to remove the new matter from the claims.

Rejection(s) under 35 U.S.C § 112, First Paragraph (Lack of Enablement)

11) Claims 17-21 are rejected under 35 U.S.C. § 112, first paragraph, as 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. This is a lack of enablement rejection.

Instant claims are evaluated based on the *Wands* analysis. Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Circ. 1988) as follows:

- The quantity of experimentation necessary (time and expense);
- The amount of direction or guidance presented;
- The presence or absence of working examples of the invention;
- The nature of the invention;
- The state of the art;
- The relative skill of those in the art;
- The predictability or unpredictability of the art; and
- The breadth of the claims.

In the instant application, the nature of the invention is related to: (a) a method of 'preventing' or 'modulating' a T cell-mediated response such as delayed type hypersensitivity (DTH) in a host; and (b) a method of 'treating' or 'preventing' any condition associated with overstimulation of T cells such as toxic shock syndrome in a human or animal; and (c) a method of 'treating' or 'preventing' any T cell lymphoproliferative disease by administering an isolated *S. aureus* Map protein having the amino acid sequence of SEQ ID NO: 2. Although the relative skill of those in the art is high, 'preventing' a T cell-mediated response such as delayed type hypersensitivity (DTH) in a human or non-human host, 'preventing' or 'treating' any generic condition associated with overstimulation of T cells, or toxic shock syndrome in particular in a human or an animal, and 'preventing' or 'treating' any generic T cell lymphoproliferative disease, by administering an isolated *S. aureus* Map protein having the amino acid sequence of SEQ ID NO: 2 is highly unpredictable. The limitations in the instant claims, 'a T cell-mediated response', 'a condition associated with overstimulation of T cells', and 'a T cell lymphoproliferative disease' are so broad that they encompass within their scope T cell-mediated responses, T cell lymphoproliferative diseases, and conditions associated with overstimulation of T cells, due to

diverse microbial and non-microbial etiology. The T cell-mediated response, including DTH, occurs in various non-*S. aureus* infections. The paragraph bridging pages 11 and 12 of the specification exemplifies certain serious T cell lymphoproliferative diseases such as lymphoma, T chronic and acute lymphoproliferative leukemia, Sezary's syndrome, T cell type of hairy cell leukemia, HTLV-associated adult T cell leukemia/lymphoma and non-Hodgkin's lymphoma. A review of the specification indicates that the enabling disclosure is limited to a showing that recombinant DbpA-immunized mice upon administration of 100 micrograms of recombinant Map19 showed reduced DTH as measured by footpad swelling (see pages 21 and 22; and Table IV). There is no predictability that these data can be extrapolated to an *in vivo* situation for 'preventing' a non-DbpA-induced T cell-mediated response or DTH in a human or animal host. The second half of pages 27, 30 and 23 of the specification provide data that are limited to an *in vitro* showing that the recombinant Map19 inhibited the *in vitro* proliferation of *Borrelia burgdorferi*-specific T cell line BAT 2.2. This showing is insufficient to enable a method of 'treating' or 'preventing' *in vivo*, any generic condition associated with *Borrelia burgdorferi*-specific or *Borrelia burgdorferi*-nonspecific overstimulation of T cells in a human or an animal patient by administering an isolated Map protein having the amino acid sequence of SEQ ID NO: 2 in the recited amount to treat or prevent said generic condition. The specification lacks correlation between *in vitro* results and *in vivo* results with regard to the methods claimed in claims 19-21. This is critically important because the art recognizes the difficulty in predicting *in vivo* pharmaceutical activity of a bacterial protein based on *in vitro* experimentation. See lines 38-47 in column 2 of Wainwright *et al.* (US 6,222,021). The *in vivo* environment of a host, or a human or animal patient, includes several active cellular and humoral host immune elements and microbial or non-microbial products, including those that can inhibit or neutralize the biologic effects of the administered Map19 protein of SEQ ID NO: 2. The properties of the Map protein of SEQ ID NO: 2 including cross-reactivity with host antigens, rate of clearance from blood or other systems, bioavailability, *in vivo* localization etc. are variable parameters which can present obstacles to successful *in vivo* treatment or prevention. There is no data within the instant specification correlative to *in vivo* therapeutic or prophylactic effects in the generally recited 'condition' or 'disease'. One cannot simply extrapolate the data to an *in vivo* pathological system to show that the recited protein is useful for 'treating' a generic T

cell-mediated response in any host; for 'treating' or 'preventing' a serious pathological condition associated with overstimulation of T cells, such as, toxic shock syndrome that occurs following infection by wild-type *S. aureus*, or any pathological condition associated with overstimulation of T cells other than toxic shock syndrome, or any generic associated with overstimulation of T cells; and for 'treating' or 'preventing' T cell lymphoproliferative diseases, including such as lymphoma, T chronic and acute lymphoproliferative leukemia, Sezary's syndrome, T cell type of hairy cell leukemia, HTLV-associated adult T cell leukemia/lymphoma and non-Hodgkin's lymphoma. There is no evidence showing that T cell lymphoproliferative disease conditions as serious as thymoma, T lymphoblastic lymphoma, T chronic and acute lymphoproliferative leukemia, Sezary's syndrome, T cell type of hairy cell leukemia, HTLV-associated Japanese, Caribbean and American adult T cell leukemia/lymphoma and non-Hodgkin's lymphoma, or conditions associated with overstimulation of T cells in humans or animals such as toxic shock syndrome, are 'treated' or 'prevented' in a human or animal host or patient by administering an isolated *S. aureus* Map19 protein having the amino acid sequence of SEQ ID NO: 2. The specification states that: (a) 'recombinant Map or formulations thereof as described above 'may' have tremendous potential therapeutic value in a wide variety of clinical and pathological conditions'; (b) 'certain T cell lymphoproliferative disease 'may be potentially treated' with Map'; (c) 'Therapeutic applications for Map 'may' also be available in various conditions resulting from microbial infection'; and (d) 'the Map compositions in accordance with the present invention 'may be' useful in treatment of T cell proliferative conditions such as poison ivy'. These statements suggest that the Map protein of the amino acid sequence SEQ ID NO: 2 has not, as yet, been shown to 'prevent', 'modulate' or 'treat' all the encompassed T cell lymphoproliferative diseases and conditions associated with overstimulation of T cells in a human or non-human patient or host, and DTH or non-DTH T cell mediated response due to any microbe or cause. The operability of the claimed methods in a host, or human or animal patient, is merely speculated, but not demonstrated. This is important because 'prevention' or 'treatment' of any random T cell-mediated response, any random condition associated with overstimulation of T cells, and any random T cell lymphoproliferative disease in a human or non-human host or patient by administering a bacterial component is not predictable, absent concrete evidence. Clearly, there is lack of direction and guidance for a skilled artisan to practice the

instantly claimed methods. Without specific guidance or direction, without convincing evidence and/or working examples, one of ordinary skill in the art would not be able to reproducibly practice the instant invention as claimed, without undue experimentation due to the therapeutic or prophylactic unpredictability associated with administration of bacterial components, the broad scope of protection sought in the claims, and the quantity of experimentation necessary. The instant specification lacks probative evidence enabling the instantly claimed methods and therefore, the instant claims are viewed as not meeting the enablement provisions of 35 U.S.C. § 112, first paragraph.

Rejection(s) under 35 U.S.C § 112, Second Paragraph

12) Claims 17-21 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant(s) regards as the invention.

(a) Claims 1, 19 and 21 are vague, indefinite in the limitation 'according to SEQ ID NO: 2'. For the purpose of distinctly claiming the subject matter, it is suggested that Applicants replace the limitation with --as set forth in SEQ ID NO: 2--.

(b) Claim 20 is incorrect and/or lacks proper antecedence in the recitation: 'A method according to Claim 19'. For proper antecedence, it is suggested that Applicants replace the recitation with --The method according to claim 19--.

(c) Claims 17, 19 and 21 are vague in the recitation: 'having an amino acid sequence ..... SEQ ID NO: 2'. For the purpose of distinctly claiming the subject matter, it is suggested that Applicants replace the limitation with -- having the amino acid sequence ..... SEQ ID NO: 2--.

(d) Claim 19 has improper antecedence in the limitation: 'the host' (see lines 2 and 3) because there is no earlier recitation of 'a host' in the claim.

(e) Claim 21 has improper antecedence in the limitation: 'the host' (see line 2) because there is no earlier recitation of 'a host' in the claim.

(f) Claims 18 and 20, which depend from claims 17 and 19 respectively, are rejected as being indefinite because of the indefiniteness identified above in the base claim.

Remarks

13) Claims 17-21 stand rejected.

14) Applicants' amendments necessitated the new ground(s) of rejection presented in this Office action. **THIS ACTION IS MADE FINAL.** Applicants are reminded of the extension of time policy as set forth in 37 C.F.R 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

15) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center, which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The Fax number for submission of amendments, responses or papers is (571) 273-8300.

16) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.Mov. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

17) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (571) 272-0864.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

April, 2005

S. DEVI, PH.D.
PRIMARY EXAMINER